

U.S. 10/088,724  
Your ref. 082377-000000US  
Our ref. KUV-102DPIPT1-US

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Appendix 1: Proposed claim amendments

1. (Previously presented) An isolated polypeptide that suppresses neuronal death associated with Alzheimer's disease having an amino acid sequence of Formula (I):

Pro-X<sub>n1</sub>-(Cys/bXaa)-(Leu/Arg)-X<sub>n2</sub>-Leu-Thr-(Gly/Ser)-X<sub>n3</sub>-Pro (I)

(SEQ ID NO: 63)

wherein "Cys/bXaa" indicates Cys or a basic amino acid; "(Leu/Arg)" indicates Leu or Arg; "(Gly/Ser)" indicates Gly or Ser; and X<sub>n1</sub>, X<sub>n2</sub>, and X<sub>n3</sub> independently indicate arbitrary amino acid sequences not more than 10 residues in length, respectively.

2. (Previously presented) An isolated polypeptide selected from the group consisting of:

(a) a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60; and

(b) a polypeptide that suppresses neuronal death associated with Alzheimer's disease having an amino acid sequence which differs from a polypeptide of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60, in such a way that one amino acid has been substituted, deleted, inserted, or added.

3. (Canceled)

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4. (Previously presented) A fusion polypeptide comprising the polypeptide of any of claims 1 to 2 fused with one or more other polypeptides.

5. (Currently amended) An isolated DNA encoding a polypeptide selected from the group consisting of:

(a) a polypeptide that suppresses neuronal death associated with Alzheimer's disease having the amino acid sequence of Formula (I):

Pro-X<sub>n1</sub>-(Cys/bXaa)-(Leu/Arg)-X<sub>n2</sub>-Leu-Thr-(Gly/Ser)-X<sub>n3</sub>-Pro (I)

(SEQ ID NO: 63)

wherein "Cys/bXaa" indicates Cys or a basic amino acid; "(Leu/Arg)" indicates Leu or Arg; "(Gly/Ser)" indicates Gly or Ser; and X<sub>n1</sub>, X<sub>n2</sub>, and X<sub>n3</sub> independently indicate arbitrary amino acid sequences not more than 10 residues in length, respectively;

(b) a polypeptide comprising an amino acid sequence which differs from a polypeptide of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60 in which in such a way that one amino acid has been substituted, deleted, inserted, or added, in such a way that wherein the polypeptide suppresses neuronal death associated with Alzheimer's disease;

(c) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60; and

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(d) a fusion polypeptide comprising the polypeptide of (a) or (c) fused with one or more other polypeptides;

wherein the DNA does not comprise the sequence of SEQ ID NO:4.

6. (Previously presented) A vector into which a DNA encoding a polypeptide of any one of (a) to (c) is inserted:

(a) a polypeptide that suppresses neuronal death associated with Alzheimer's disease having the amino acid sequence of Formula (I);

$\text{Pro-X}_{n1}\text{-(Cys/bXaa)-(Leu/Arg)-X}_{n2}\text{-Leu-Thr-(Gly/Ser)-X}_{n3}\text{-Pro}$  (I)

(SEQ ID NO: 63)

wherein "Cys/bXaa" indicates Cys or a basic amino acid; "(Leu/Arg)" indicates Leu or Arg; "(Gly/Ser)" indicates Gly or Ser, and  $X_{n1}$ ,  $X_{n2}$ , and  $X_{n3}$  independently indicate arbitrary amino acid sequences not more than 10 residues in length, respectively;

(b) a polypeptide comprising an amino acid sequence which differs from a polypeptide of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60 in such a way that one amino acid has been substituted, deleted, inserted, or added, wherein the polypeptide suppresses neuronal death associated with Alzheimer's disease;

(c) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60; and

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(d) a fusion polypeptide comprising the polypeptide of (a) or (b) fused with one or more other polypeptides.

7. (Original) A host cell retaining the vector of claim 6.

8. (Previously presented) A method for producing the polypeptide of any one of claims 1 to 2 or a fusion polypeptide comprising the polypeptide of any one of claims 1 to 2, comprising:

culturing a host cell retaining a vector into which a DNA encoding the polypeptide of any one of claims 1 to 2, or a fusion polypeptide comprising the polypeptide of any one of claims 1 to 2 fused with one or more other polypeptides, is inserted; and

recovering an expressed polypeptide from the host cell or culture supernatant thereof.

9-12. (Canceled)

13. (Previously presented) A pharmaceutical composition comprising the polypeptide of any one of claims 1 to 2.

14-15. (Canceled)

16. (Currently amended) The pharmaceutical composition of claim 13, comprising an amount of the polypeptide effective to treat Alzheimer's disease associated with amyloid pathology or a mutation of a protein selected from the group consisting of amyloid precursor protein, presenilin-1 and presenilin-2.

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17-19 (Canceled)

20. (Previously presented)) The polypeptide of claim 1, wherein  $Xn_1$  is an amino acid sequence consisting of 3 to 5 arbitrary amino acids,  $Xn_2$  is an amino acid sequence consisting of 1 to 3 arbitrary amino acids, and  $Xn_3$  is an amino acid sequence consisting of 3 to 5 arbitrary amino acids.

21. (Previously presented) The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 101.

22. (Previously presented) The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 102.

23-26 (Canceled)

27. (Previously presented) The polypeptide of claim 2, wherein the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60.

28. (Previously presented) The DNA of claim 5, wherein  $Xn_1$  is an amino acid sequence consisting of 3 to 5 arbitrary amino acids,  $Xn_2$  is an amino acid sequence consisting of 1 to 3 arbitrary amino acids, and  $Xn_3$  is an amino acid sequence consisting of 3 to 5 arbitrary amino acids.

29. (Previously presented) The DNA of claim 5, wherein the DNA encodes a polypeptide comprising an amino acid sequence of SEQ ID NO: 101.

30. (Previously presented) The DNA of claim 5, wherein the DNA encodes a polypeptide comprising an amino acid sequence of SEQ ID NO: 102.

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31-34. (Canceled)

35. (Previously presented) The DNA of claim 5, wherein the DNA encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6 to 8, 10, 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60.

36. (Previously presented) The vector of claim 6, wherein  $X_{n1}$  is an amino acid sequence consisting of 3 to 5 arbitrary amino acids,  $X_{n2}$  is an amino acid sequence consisting of 1 to 3 arbitrary amino acids, and  $X_{n3}$  is an amino acid sequence consisting of 3 to 5 arbitrary amino acids.

37. (Previously presented) The vector of claim 6, wherein the DNA encodes a polypeptide comprising an amino acid sequence of SEQ ID NO: 101.

38. (Previously presented) The vector of claim 6, wherein the DNA encodes a polypeptide comprising an amino acid sequence of SEQ ID NO: 102.

39-42. (Cancelled)

43. (Previously presented) The vector of claim 6, wherein the DNA encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5 to 8, 10, 12, 13, 21 to 24, 26 to 29, 32, 33, 37 to 40, 46, 48, 54, and 60.

44. (Cancelled)

45. (Previously presented) A composition comprising a polypeptide of claim 2, and a carrier.

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46. (Currently amended) The pharmaceutical composition of claim 13, comprising an amount of the polypeptide effective to treat a neurodegenerative Alzheimer's disease associated with amyloid pathology or a mutation of a protein selected from the group consisting of an amyloid precursor protein, presenilin-1 and presenilin-2.

47. (Previously presented) A pharmaceutical composition comprising a vector into which a DNA encoding the polypeptide of any one of claims 1 to 2 is inserted.

48. (Currently amended) The pharmaceutical composition of claim 47, wherein the composition is suitable to treat Alzheimer's disease associated with amyloid pathology or a mutation of a protein selected from the group consisting of amyloid precursor protein, presenilin-1 and presenilin-2.

49. (Currently amended) The pharmaceutical composition of claim 47, wherein the composition is suitable to treat a neurodegenerative Alzheimer's disease associated with amyloid pathology or a mutation of a protein selected from the group consisting of an amyloid precursor protein, presenilin-1 and presenilin-2.